Cal/EPA

Cancer Potency Information

Back

New Search:

Chemical Name

Trichloroethylene

OR

CAS Number

79016

New Search

Inhalation Unit Risk (µg/cubic meter)$^{-1}$	0.000002
Inhalation Slope Factor (mg/kg-day)$^{-1}$	0.007
Oral Slope Factor (mg/kg-day)$^{-1}$	0.013
USEPA Classification	
IARC Classification	2A: The agent is probably carcinogenic to humans
Comments	A change was made on 9/24/03, see history log for explanation.
Reference	OEHHA, 2002 Technical Support Document for Describing Available Cancer Potency Factors OEHHA, 1999 Public Health Goal for Trichloroeth in Drinking Water

Air Toxics Hot Spots Program Risk Assessment Guidelines

Part II

Technical Support Document for Describing Available Cancer Potency Factors

December 2002

Secretary for Environmental Protection
California Environmental Protection Agency
Winston H. Hickox

Director
Office of Environmental Health Hazard Assessment
Joan E. Denton, Ph.D.

Technical Support Document for Describing Available Cancer Potency Factors

December 2002

California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Air Toxicology and Epidemiology Section

TRICHLOROETHYLENE

CAS No: 79-01-6

I. PHYSICAL AND CHEMICAL PROPERTIES (Fan, 1988)

Molecular weight	131.4
Boiling point	87.7° C
Melting point	-72.8° C
Vapor pressure	77 mm Hg @ 25° C
Air concentration conversion	1 ppm = 5.37 mg/m^3 @ 25° C

II. HEALTH ASSESSMENT VALUES

Unit Risk Factor: 2.0 E-6 $(\mu g/m^3)^{-1}$

Slope Factor: 7.0 E-3 $(mg/kg\text{-}day)^{-1}$

[Male mouse hepatocellular adenoma and carcinoma incidence, female mouse lung adenocarcinoma and malignant lymphoma incidence (Bell *et al.*, 1978; Henschler *et al.*, 1980; Fukada *et al.*, 1983; Maltoni *et al.*, 1986). Cancer unit risks calculated using a linearized multistage procedure, metabolized dose of TCE determined using a physiologically-based pharmacokinetic (PBPK) model, geometric mean of unit risks (CDHS, 1990a).]

III. CARCINOGENIC EFFECTS

Human Studies

Hardell *et al.* (1981) conducted a retrospective study of 169 men, aged 25 to 85 years in Umea, Sweden, between 1974 and 1978 for histologically confirmed malignant lymphoma. Sixty cases had Hodgkin's disease and 109 had non-Hodgkin's lymphoma. Seven cases and three controls reported high-grade exposure to TCE (odds ratio of 7.88). When compared with 162 cases and 335 controls that were not exposed to high-grade levels of TCE, but including those persons exposed to other chemicals and low-grade levels of TCE, the odds ratio dropped to 4.8, but remained significant ($p < 0.05$, chi-squared test). This study yielded an estimate of the relative risk of developing malignant lymphoma that is more than seven times greater for those who recall a high-grade exposure to TCE compared with those that report no exposure to phenoxy acids, chlorophenols, or organic solvents.

Imperial Chemical Industries conducted a retrospective study of 95 primary liver cancer cases diagnosed between 1951 and 1977 in England (Paddle, 1983). Paddle calculated the expected number of cases of primary liver cancer among workers from 1951 to 1977 to be about 0.3.

Axelson *et al.* (1978) who performed a mortality analysis of a cohort of workers occupationally exposed to TCE from 1955 to 1975, revealed 49 deaths from all causes (62 were expected using Swedish national death-rates). No significant elevated risk of tumor-related deaths was observed. The

study size was probably too small to detect a positive association between exposure to TCE and specific cancer deaths. Therefore, an upper bound on potential cancer risk of TCE to humans cannot be estimated on the basis of data from this study.

US EPA (1985) reported an historical cohort study by Malek *et al.* (1979) of 57 dry cleaners who used TCE as a cleaning solvent. Exposure to TCE was confirmed by urine analyses of the metabolite trichloroacetic acid (TCA). The follow-up time ranged from 5 to 50 years with a median greater than 20 years. The 6 cases of cancer observed were not significantly ($p < 0.05$) different from the number expected in the general population. The small size of the cohort severely limited the power of the study to detect a significant increase in cancer incidence.

Tola *et al.* (1980) established a cohort of 2117 workers (1148 men, 969 women) who had been occupationally exposed to TCE at some time between 1963 and 1976. The observed number of deaths (58) was lower than those expected (84.3). The percentage of deaths attributable to cancer among the workers (11/58 = 19%) was slightly greater than expected, but the difference was not significant ($p > 0.05$). The results from this study did not demonstrate an increased tumor incidence among workers exposed to TCE relative to that of the general Finnish population. Several limitations, such as unknown duration of exposure to TCE and exposure to other organic solvents, prevent a firm conclusion.

Shindell and Ulrich (1985) studied a cohort of 2,646 people who had worked at least 3 months between 1957 and 1983 at a facility that used TCE as a degreasing agent. The cohort showed a healthy worker effect (Standard Mortality Ratio = 0.79 for all causes of death) and much lower levels of heart disease and hypertension than the general population.

There are a number of cohort studies on workers exposed to TCE as a dry-cleaning solvent. Use of TCE as a dry-cleaning solvent began in the 1930's and waned in the 1960's (Waters *et al.*, 1977). Cohort studies of dry-cleaning workers have been reviewed in the past (IARC, 1979; Apfeldorf and Infante, 1981). The value of these studies is greatly limited by an undefined exposure to TCE and is confounded by exposure to other dry-cleaning agents such as tetrachloroethylene, carbon tetrachloride, and petroleum solvents.

Significant ($p < 0.05$) increases in the incidence of cancers of the lung, cervix, and skin contributed to an overall significant excess of cancer deaths among 330 deceased laundry and dry-cleaning workers (Blair *et al.*, 1979). This cohort also showed a slight increase in leukemia, liver, and kidney cancer, and a deficit of breast cancer compared to that expected. The authors warn that the cohort mortality pattern may reflect inherent biases, such as socioeconomic status and smoking, and should be interpreted cautiously.

Katz and Jowett (1981) reported a significant elevated risk for cancers of the kidney ($p < 0.05$) and genitals ($p < 0.01$) in a cohort of 671 deceased white female laundry and dry-cleaning workers. The cohort also exhibited smaller excesses of lymphosarcoma, bladder cancer, and skin cancer. An increase in cervical cancer disappeared when compared to low-wage controls.

A mortality analysis of a cohort of metal platers and polishers revealed significantly ($p < 0.05$) higher proportionate mortality ratios for esophageal and liver cancer deaths relative to a general white male population (Blair, 1980). The positive results were, however, confounded by occupational exposure to known carcinogens, including chromium, nickel, and other metals, along with acids and other solvents.

Animal Studies

The National Cancer Institute (NCI, 1976) study was the first major long-term cancer bioassay of TCE. TCE was administered by gavage 5 days/week for 78 weeks to B6C3F$_1$ mice and Osborne-Mendel rats of both sexes (n = 50). The industrial grade of TCE used contained 1,2-epoxybutane (0.19%), ethyl acetate (0.04%), epichlorohydrin (0.09%), N-methylpyrrole (0.02%), and diisobutylene (0.03%) as stabilizers.

Male mice received initial daily doses of 2000 mg/kg of body weight in the high-dose group and 1000 mg/kg in the low-dose group. Dose levels were increased during the course of the study resulting in corresponding experimental time-weighted average (TWA) doses of 2339 and 1169 mg/kg. Initial doses to female mice were 1400 and 700 mg/kg, and the corresponding experimental TWA doses were 1739 and 869 mg/kg. For rats, high-dose groups of both sexes initially received 1300 mg/kg, but a lower TWA dose of 1097 mg/kg. The low-dose groups initially received 650 mg/kg, but a lower TWA dose of 549 mg/kg.

Higher incidences of hepatocellular carcinoma in mice were statistically significant in both high- (31/48, $p < 0.001$) and low-dose (26/50, $p = 0.004$) males and high-dose females (11/47, $p = 0.008$) relative to the matched controls.

In contrast to the positive results in the mouse study, analysis of tumor incidences in rats showed no significant difference in specific or total tumors between treated and control groups.

Questions have been raised about the possible impact of the epichlorohydrin (ECH) impurity in the TCE used. While it is possible that ECH contributed to the observed increased tumor incidence in TCE-exposed mice in the NCI (1976) bioassay, it is unlikely that ECH was responsible for all or most of the increased incidence observed. US EPA (1985) also noted that TCE-treated animals in the NCI (1976) experiments were housed in the same rooms as animals treated with other compounds but considered it unlikely that other compounds were responsible for the observed response.

To address the question of contaminant effects on the results of the 1976 NCI mouse study, the National Toxicology Program (NTP, 1983) repeated the carcinogenicity studies in B6C3F$_1$ mice and F344/N rats. The TCE contained no epichlorohydrin and was stabilized with 8 ppm diisopropylamine. Treated mice and high-dose rats received 1000 mg/kg TCE 5 days/week. Low-dose rats received 500 mg/kg TCE 5 days/week. The dosing period lasted 103 weeks.

The incidences of renal tubular-cell adenocarcinoma in male rats dosed with TCE were not significantly different from controls. However, high-dose male rats that survived until the end of the experiment

exhibited a statistically significant higher incidence (3/16) of renal tubular-cell adenocarcinoma than the study controls (0/33) or F344/N male rats historical vehicle gavage controls (3/748). The NTP (1983) considers these results equivocal and "inadequate to evaluate the presence or absence of a carcinogenic response" of these rats to TCE. Significantly higher incidences of hepatocellular carcinoma in dosed male mice (30/50, $p < 0.001$) and dosed female mice (13/49, $p < 0.05$) relative to those of their controls (8/48 and 2/48, respectively) confirmed the positive results of the 1976 NCI mouse study. Dosed female mice were also found to have a statistically significant ($p < 0.05$) increase in the incidence of hepatocellular adenomas (8/49) relative to that of the controls (2/48). This bioassay provided evidence that epichlorohydrin is not needed to induce hepatocarcinogenesis in $B6C3F_1$ mice.

In another NTP study (1988), 4 strains of rat (ACI, August, Marshall, and Osborne-Mendel) received high (1000 mg/kg) or low (500 mg/kg) daily doses of TCE in corn oil by gavage 5 days/week for 103 weeks. The TCE used contained no epichlorohydrin. Test groups consisted of 50 animals of each sex. An increased incidence of renal tubular cell tumors was observed in dosed animals, and an increased incidence of interstitial cell tumors of the testes was observed in dosed Marshall rats. Results of audits conducted in 1983 and 1984, revealed problems with the laboratory conducting the study (NTP, 1988) making interpretation of the bioassay results difficult.

Bell *et al.* (1978) reported the results of a study in which Charles River rats (120/group) and $B6C3F_1$ mice (140/group) were exposed to TCE vapor at concentrations of 100, 300, or 600 ppm for 6 hours/day, 5 days/week, for 104 weeks. Animals were sacrificed upon termination of treatment. The test chemical was greater than 99% pure but contained impurities such as diisobutylene, butylene oxide, ethyl acetate, N-methylpyrrole, and epichlorohydrin.

The incidences of hepatocellular carcinoma in male mice exposed to TCE at concentrations of 100 ppm (28/95), 300 ppm (31/100), and 600 ppm (43/97) were statistically significant ($p < 0.05$, $p = 0.03$, and $p < 0.001$, respectively) when compared to controls (18/99). The level of significance increased when the incidences of both hepatocellular carcinoma and hepatocellular adenoma combined in treated versus control mice are compared by the Fisher exact test. Female mice exposed to TCE at a concentration of 600 ppm exhibited a significant ($p < 0.05$) increase in the incidence of hepatocellular adenomas and hepatocellular carcinomas combined (17/99) relative to that of the controls (8/99). No statistically significant increase in the incidence of any other tumor type was observed among the treated rats. An audit revealed marked deficiencies and flaws in both the rat and mouse studies. According to US EPA (1985), the usefulness of these bioassays is limited by deficiencies in their conduct.

Van Duuren *et al.* (1979) exposed Ha/ICR male and female mice to purified TCE by 3 different routes: skin application, subcutaneous injection, and gavage. No significant increase in any tumor was observed in treated animals by any route of administration.

Henschler *et al.* (1980) exposed 3 species of rodents (Han:NMRI mice, and Syrian hamsters) to concentrations of pure amine-based TCE at 100 and 500 ppm for 6 hours/day, 5 days/week, for 78 weeks. Neither rats, hamsters, nor male mice had significantly increased tumor incidence. Dosed female mice, however, exhibited significantly ($p < 0.05$) higher incidences of malignant lymphoma

relative to that of the controls which may be due to immunosuppression by TCE or some other nonspecific agent (US EPA, 1985).

In a study by Fukuda *et al.* (1983), female Sprague-Dawley rats and female ICR mice were exposed to concentrations of 50, 150, and 450 ppm of reagent grade TCE for 7 hours/day, 5 days/week, for 104 weeks (49-51 animals/test group). Chemical analysis revealed the test sample TCE, 99.824% pure, to contain impurities such as carbon tetrachloride, benzene, epichlorohydrin, and 1,1,2-trichloroethane in the vapor phase. The incidence of lung adenocarcinomas among mice in the 2 higher exposure groups (150 ppm, 8/50; 450 ppm, 7/46) was significantly ($p < 0.05$) higher than that of the controls (1/49), but the incidence was not dose-related. The incidence of total lung tumors (adenomas and adenocarcinomas combined) in exposed mice was not significantly different from that of the controls. Statistical analysis of the tumor incidences among rats showed no significant increases or trends.

Henschler *et al.* (1984) tested different samples of TCE with or without epichlorohydrin (ECH) and/or 1,2-epoxybutane, in groups of 50 5-week-old male or female ICR/Ha-Swiss mice. Treated animals received TCE, with or without epoxides, by corn oil gavage 5 days/week for 18 months. Males received 2400 mg/kg, while females received 1800 mg/kg. All doses were reduced after the 40th week giving an experimental TWA daily doses of 1900 mg/kg for males and 1400 mg/kg for females.

Mice dosed with pure TCE did not exhibit a statistically significant increase in the incidence of any tumor type. The administration of TCE with 0.8% ECH or both 0.25% ECH and 0.25% 1,2-epoxybutane was associated with a significant ($p < 0.05$) increase in forestomach papillomas or carcinomas in both sexes. These predicted increased risks from ECH more than account for the observed increased incidence of forestomach tumors cited above. Thus, results from this study support the hypothesis that ECH may be the proximate cause of increased tumor incidence observed in some studies of rodents exposed to ECH-stabilized TCE.

Maltoni *et al.* (1986) reported the results of a series of 8 TCE carcinogenicity experiments performed between 1976 and 1983, using mice and rats. In bioassay BT301, TCE was administered by stomach tube to Sprague-Dawley rats (30/sex/group) at dose levels of 50 or 250 mg/kg, 4 to 5 days/weeks, for 52 weeks. No significant increase in any tumor was observed in treated animals. This was probably due to the dosing period of 52 weeks which was less than a potential lifetime exposure.

Two short-term inhalation bioassays were conducted by Maltoni *et al.* (1986) with Sprague-Dawley rats (BT302) and Swiss mice (BT303). The animals were exposed to 100 or 600 ppm TCE for 7 hours/day, 5 day/weeks, for 8 weeks. No statistically significant effect was observed.

Bioassays BT304-bis were two similar long-term inhalation experiments whose results were combined and evaluated together. Sprague-Dawley rats were exposed to either 100, 300 or 600 ppm TCE for 7 hours/day, 5 days/week, for 104 weeks. A statistically significant, exposure-related increase in the incidence of Leydig cell tumors of the testes was observed in treated rats: 31/130 at 600 ppm, 30/130 at 300 ppm and 16/130 at 100 ppm, compared to 6/135 in the control group. Five of 260 rats

exposed to 600 ppm TCE developed kidney adenocarcinomas that, although lacking statistical significance, must be considered biologically significant due to their rarity.

In experiment BT305, Swiss mice were exposed to TCE at a concentration of 100, 300 or 600 ppm for 7 hours/day, 5 days/week, for 78 weeks. Males exposed to the 2 higher levels showed statistically significant increases in the incidence of pulmonary tumors (27/90 at 600 ppm, 23/90 at 300 ppm) relative to that of the control group (11/90). Males exposed to 600 ppm TCE also had a higher frequency of hepatomas (13/90, $p < 0.05$) than that of controls (4/90). Females did not show any significant response to TCE exposure in this bioassay.

Bioassays BT306 and BT306-bis were both conducted with B6C3Fl mice under similar exposure conditions as above. A dose-related increase in the incidence of pulmonary tumors was observed in females but was significant ($p < 0.05$) only at 600 ppm (15/90) relative to the control group (4/90).

IV. DERIVATION OF CANCER POTENCY

Basis for Cancer Potency

Based on their designation of "limited evidence" of carcinogenicity in animals and "inadequate evidence" of carcinogenicity in humans, IARC (1984) determined that TCE cannot be classified as to its carcinogenicity to humans. US EPA placed TCE in Group B2, a probable human carcinogen (US EPA, 1985). CDHS staff reviewed the literature and disagreed with IARC's conclusion. CDHS considers TCE to be carcinogenic and not to have a threshold for carcinogenicity (CDHS, 1990a).

A quantitative risk assessment for TCE was conducted by CDHS (1990a) using the dose-response data for carcinogenicity from four inhalation studies in mice (Bell *et al.*, 1978; Henschler *et al.*, 1980; Fukada *et al.*, 1983; Maltoni *et al.*, 1986).

Methodology

The metabolized dose for TCE for each of the studies evaluated was determined using a physiologically-based pharmacokinetic model (PBPK) and used for the calculation of carcinogenic potency. Because absorbed TCE is completely metabolized, metabolized dose mirrors applied dose. The metabolized dose of TCE was included because it takes into account uptake and distribution factors. The data obtained for uptake and distribution factors are in good agreement with experimental results obtained with human volunteers. Interspecies variation was accounted for by utilizing surface area scaling.

Carcinogenic responses in the inhalation studies included increased incidences of hepatocellular carcinoma and adenoma in male mice and increased incidences of lung adenocarcinomas and malignant lymphomas in female mice. Since most tumors were discovered at the time of sacrifice rather than at the time of their appearance, the GLOBAL79 and GLOBAL86 computer programs for the linearized multistage modes, without a time-to-tumor factor, were used for the low-dose risk assessment. The above adjustments to the animals' exposure results in a lifetime time-weighted average dose, either

applied or metabolized. The range of 95% upper confidence limit (UCL) potency estimates (q_1*) obtained using the human equivalent applied and metabolized doses and the tumor incidences in the four inhalation studies notes above is 0.006 to 0.098 $(mg/kg\text{-}day)^{-1}$. Based on the same data, the individual risk for a 70-year lifetime exposure of a 70 kg person breathing 20 m^3 per day of ambient air containing 1 $\mu g/m^3$ (0.19 ppb) of TCE is 8×10^{-7} to 1×10^{-5}. A best estimate of the unit risk was obtained by taking the geometric mean of the unit risks from the four inhalation studies. From the metabolized dose approach a unit risk of 2.0×10^{-6} $(\mu g/m^3)^{-1}$ was obtained, and from the applied dose a unit risk of 3.0×10^{-6} $(\mu g/m^3)^{-1}$ was obtained. CDHS (1990b) chose the cancer unit risk value of 2.0×10^{-6} $(\mu g/m^3)^{-1}$ calculated using the metabolized dose approach as the "best value" for TCE inhalation cancer unit risk

Table 1: Dose-response data used by CDHS (1990a) in quantitative risk assessment for trichloroethylene exposure[1]

Study Species / sex Strain	Tumor Type	Daily experimental applied concentration	LTWA Metabolized Dose[2] (mg/kg-day)	Tumor Incidence[3]
Bell *et al.*, 1978	hepatocellular	0 ppm – 6 hr	0	20/99
Mice (male)	carcinoma or	100 ppm – 6 hr	42.3	35/95
$B6C3F_1$	adenoma	300 ppm – 6 hr	127	38/100
		600 ppm – 6 hr	254	53/97
Henschler *et al.*, 1980	malignant	0 ppm – 6 hr	0	9/29
Mice (female)	lymphoma	100 ppm – 6 hr	33.2	17/30
Han:NMRI		500 ppm – 6 hr	166	18/28
Fakuda *et al.*, 1983	lung	0 ppm – 7 hr	0	1/49
Mice (female)	adenocarcinoma	50 ppm – 7 hr	25.8	3/50
ICR		150 ppm – 7 hr	77.4	8/50
		450 ppm – 7 hr	232	7/46
Maltoni *et al.*, 1986	malignant	0 ppm – 7 hr	0	4/90
Mice (male)	hepatoma	100 ppm – 7 hr	35.3	2/90
Swiss		300 ppm – 7 hr	106	8/90
		600 ppm – 7 hr	212	13/90

[1]Source: CDHS (1990a).

[2]Lifetime, time-weighted-average metabolized dose.

[3]Tumor incidence denominator excludes animals dying before the occurrence of the first corresponding tumor type observed in the NCI (1976) and NTP (1983) studies. See CDHS (1990a) for more detail.

V. REFERENCES

Apfeldorf R and Infante PF. 1981. Review of epidemiologic study results of vinyl chloride-related compounds. Environ Health Perspect 41:221-226.

Axelson O, Andersson K, Hogstedt C, Holmberg B, Molina G and de Verdier A. 1978. A cohort study on trichloroethylene exposure and cancer mortality. J Occup Med 41:221-226.

Bell ZG, Olson KJ and Benya TJ . 1978. Final Report of Audit Findings of the Manufacturing Chemists Association (MCA): Administered Trichloroethylene (TCE) Chronic Inhalation Study at Industrial Bio-Test Laboratories, Inc., Decatur, IL. Unpublished study reported in US EPA (1985).

Blair A, Decoufle P and Grauman D . 1979. Causes of death among laundry and dry cleaning workers. Am J Public Health 69:508-511.

Blair A. 1980. Mortality among workers in the metal polishing and plating industry, 1951-1969. J Occup Med 22:158-162.

California Department of Health Services (CDHS) 1990a. Health Effects of Trichloroethylene. Air Toxicology and Epidemiology Section, Berkeley, CA.

California Department of Health Services (CDHS) 1990b. Risk Specific Intake Level for Trichloroethylene. Reproductive and Cancer Hazard Assessment Section, Health Hazard Assessment Division, Berkeley, CA.

Fan A. 1988. Trichloroethylene: water contamination and health risk assessment. Rev Environ Contam Toxicol 101:55-92.

Fukuda K, Takemoto K and Tsuruta H. 1983. Inhalation carcinogenicity of trichloroethylene in mice and rats. Ind Health 21:243-254.

Hardell L, Eriksson M, Lenner P and Lundgren E. 1981. Malignant lymphoma and exposure to chemicals, especially organic solvents, chlorophenols and phenoxy acids: a case-control study. Br J Cancer 43:169-176.

Henschler D, Elsasser H, Romen W and Eder E. 1984. Carcinogenicity study of trichloroethylene, with and without epoxide stabilizers, in mice. J Cancer Res Clin Oncol 107:149-156.

Henschler DH, Romen W, Elsasser HM, Reichert D, Eder E and Radwan Z. 1980. Carcinogenicity study of trichloroethylene by longterm inhalation in three animal species. Arch Toxicol 43:237-248.

International Agency for Research on Cancer (IARC). 1979. Trichloroethylene. In: Some Halogenated Hydrocarbons. Vol. 20. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. IARC, Lyon, France, pp. 545-572.

International Agency for Research on Cancer (IARC). 1982. Trichloroethylene. In: Chemicals, Industrial Processes and Industries Associated with Cancer in Humans. IARC Monographs on the Evaluation of the Carcinogenic Risks of Chemicals to Humans. Suppl. 4. IARC, Lyon, France, pp. 247-248.

Katz RM and Jowett D. 1981. Female laundry and dry cleaning workers in Wisconsin: a mortality analysis. Am J Public Health 71:305-307.

Malek B, Krcmarova B and Rodova O. 1979. An epidemilogical study of hepatic tumor incidence in subjects working with trichloroethylene. II. Negative results of retrospective investigations in dry-cleaners. Pracov Lek 31:124-126.

Maltoni C, Lefemine G and Cotti G. 1986. Archives of Research on Industrial Carcinogenesis. Volume V. Experimental Research on Trichloroethylene Carcinogenesis. Princeton Scientific Publishing Co., Inc., Princeton, NJ.

National Cancer Institute (NCI) 1976. Carcinogenesis Bioassay of Trichloroethylene, NCI-CG-TR-2. DHEW Pub. No. (NIH) 76-802. U.S. Government Printing Office, Washington, DC.

Hazardous Substance Data Bank (HSDB) (Internet version) 1998. National Library of Medicine, Bethesda MD.

National Toxicology Program (NTP) 1983. NTP technical report on the carcinogenesis studies of trichloroethylene (without epichlorohydrin) CAS No. 79-01-6 in F344/N rats and B6C3F1 mice (Gavage studies): Draft Report. NIH Pub. No. 83-1799. National Toxicology Program (NTP).

National Toxicology Program (NTP) 1988. Toxicology and carcinogenesis studies of trichloroethylene (CAS No. 79-01-6) in four strains of rats (ACI, August, Marshall, Osborne-Mendel) (Gavage studies). National Toxicology Program Technical Report Series No. 273. NIH Pub. No. 88-2529. U.S. Department of Health and Human Services.

Paddle GM. 1983. Incidence of liver cancer and trichloroethylene manufacture: joint study by industry and a cancer registry. Br Med J 286:846.

Shindell S and Ulrich S. 1985. A cohort study of employees of a manufacturing plant using trichloroethylene. J Occup Med 27:577-579.

Tola S, Vilhunen R, Jarvinen E and Korkala M-L. 1980. A cohort study on workers exposed to trichloroethylene. J Occup Med 22:737-740.

U.S. Environmental Protection Agency (US EPA) 1985. Health Assessment Document for Trichloroethylene. EPA/600/8-82/006F. Office of Health and Environmental Assessment, Washington, DC.

Van Duuren BL, Goldschmidt BM, Loewengart G, Smith AC, Melchionne S, Seidman I and Roth D. 1979. Carcinogenicity of halogenated olefinic and aliphatic hydrocarbons in mice. J Natl Cancer Inst 63:1433-1439.

Waters E, Gerstner H and Huff H. 1977. Trichloroethylene. I. An overview. J Toxicol Environ Health 2:271-307.